

10691095

L9 ANSWER 1 OF 2 PHIN COPYRIGHT 2009 Informa UK Ltd on STN

AN 2005:14312 PHIN

DED 19 Sep 2005

TI PHARMAPROJECTS - New Neurological Products for week ending 16 September 2005

SO Scrip-Online-plus (2005)

DT Newsletter

FS FULL

L9 ANSWER 2 OF 2 DRUGU COPYRIGHT 2009 THOMSON REUTERS on STN

AN 112843 DRUGU

FS Registry

DDRN DR0148914

DDN **ABT-769**

CT ANTICONVULSANTS; TRIAL-PREP.

SS AMINOACID; C-AMIDE; CYCLOPROPANE; SPIRO; CYCLOHEXANE

=> dup rem

ENTER L# LIST OR (END):17

DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGMONO2, IMSPRODUCT, KOSMET, NUTRACEUT, PCTGEN, PHARMAML, USGENE'.

ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE

PROCESSING COMPLETED FOR L7

L10 5 DUP REM L7 (13 DUPLICATES REMOVED)

=> d l10 1-5 ibib, kwic

L10 ANSWER 1 OF 5 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN  
DUPLICATE 1

ACCESSION NUMBER: 2005:510269 BIOSIS

DOCUMENT NUMBER: PREV200510298067

TITLE: Preclinical profiling and safety studies of **ABT-769**: A compound with potential for broad-spectrum antiepileptic activity.

AUTHOR(S): Giardina, William J.; Dart, Michael J.; Harris, Richard R.; Bitner, Robert S.; Radek, Richard J.; Fox, Gerard B.; Chemburkar, Sanjay R.; Marsh, Kennan C.; Waring, Jeffrey F.; Hui, Julia Y.; Chen, Jinhua; Curzon, Peter; Grayson, George K.; Komater, Victoria A.; Ku, Yiyin; Lockwood, Mark; Miner, Holly M.; Nikkel, Arthur L.; Pan, Jia Bao; Pu, Yu-Ming; Wang, Lei; Bennani, Youssef; Durmuller, Niklaus; Jolly, Robert; Sullivan, James P.; Roux, Sylvain; Decker, Michael W. [Reprint Author]

CORPORATE SOURCE: Abbott Labs, Dept R4N5, Bldg AP 9A-3, 100 Abbott Pk Rd, Abbott Pk, IL 60064 USA  
michael.w.decker@abbott.com

SOURCE: Epilepsia, (SEP 2005) Vol. 46, No. 9, pp. 1349-1361.  
CODEN: EPILAK. ISSN: 0013-9580.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 23 Nov 2005

Last Updated on STN: 23 Nov 2005

TI Preclinical profiling and safety studies of **ABT-769**: A compound with potential for broad-spectrum antiepileptic activity.

AB Purpose: The objective of this study was to characterize the antiseizure and safety profiles of **ABT-769** [(R)-N-(2-amino-2-oxoethyl)spiro[2,5]octane-1-carboxamide]. Methods: **ABT-**

**769** was tested for protection against maximal electroshock and pentylenetetrazol-induced seizures in the mouse and for suppression of electrically kindled amygdala seizures and spontaneous absence-like seizures in the rat. The central nervous system safety profile was evaluated by using tests of motor coordination and inhibitory avoidance. . . . toxicity was assessed in vitro by using a mitochondrial fatty acid beta-oxidation assay. Teratogenic potential was assessed in the mouse. Results: **ABT-769** blocked maximal electroshock, subcutaneous pentylenetetrazol and intravenous pentylenetetrazol-induced seizures with median effective dose (ED50) values of 0.25, 0.38, and 0.11 mmol/kg, p.o., respectively. No tolerance was evident in the intravenous pentylenetetrazol test after twice-daily dosing of **ABT-769** (0.3 mmol/kg, p.o.) for 4 days. **ABT-769** blocked absence-like spike-wave discharge (ED50, 0.15 mmol/kg, p.o.) and shortened the cortical and amygdala afterdischarge duration of kindled seizures (1 and 3 mmol/kg, p.o.). The protective indices (ED50 rotorod impairment/ED50 seizure protection) were 4.8, 3.2, and 10.9 in the maximal electroshock, subcutaneous pentylenetetrazol and intravenous pentylenetetrazol seizure tests, respectively. **ABT-769** did not affect inhibitory avoidance performance (0.1-1 mmol/kg, p.o.). **ABT-769** did not affect mitochondrial fatty acid beta-oxidation or induce neural tube defects. Conclusions: **ABT-769** is an efficacious antiseizure agent in animal models of convulsive and nonconvulsive epilepsy and has a favorable safety profile. **ABT-769** has a broad-spectrum profile like that of valproic acid. Its profile is clearly different from those of carbamazepine, phenytoin, lamotrigine, . . .

- IT . . .  
 Toxicology; Nervous System (Neural Coordination)  
 IT Parts, Structures, & Systems of Organisms  
 liver: digestive system; amygdala: nervous system  
 IT Diseases  
seizure: nervous system disease, drug therapy,  
 chemically-induced, pathology  
Seizures (MeSH)  
 IT Chemicals & Biochemicals  
 fatty acid; pentylenetetrazol: toxin; **ABT-769**  
 [[(R)- N-(2 amino-2-oxoethyl)spiro[2,5]octane-1-carboxamide]]:  
 anticonvulsant-drug, pharmacodynamics, safety, efficacy, adverse  
 effects, dosage; valproic acid: central depressant-drug,  
 tranquilizer-drug, anticonvulsant-drug, enzyme inhibitor-drug
- L10 ANSWER 2 OF 5 Elsevier Biobase COPYRIGHT 2009 Elsevier Science B.V. on  
 STN
- ACCESSION NUMBER: 2006175004 ESBIOBASE  
 TITLE: Preclinical profiling and safety studies of **ABT-769**: A compound with potential for broad-spectrum antiepileptic activity  
 AUTHOR(S): Giardina, William J.; Dart, Michael J.; Harris, Richard R.; Bitner, Robert S.; Radek, Richard J.; Fox, Gerard B.; Chemburkar, Sanjay R.; Marsh, Kennan C.; Waring, Jeffrey F.; Hui, Julia Y.; Chen, Jinhua; Curzon, Peter; Grayson, George K.; Komater, Victoria A.; Ku, Yiyin; Lockwood, Mark; Miner, Holly M.; Nikkel, Arthur L.; Pan, Jia Bao; Pu, Yu-Ming; Wang, Lei; Bennani, Youssef; Jolly, Robert; Sullivan, James P.; Decker, Michael W.; Durmuller, Niklaus; Roux, Sylvain  
 CORPORATE SOURCE: Giardina, William J.; Dart, Michael J.; Harris, Richard

R.; Bitner, Robert S.; Radek, Richard J.; Fox, Gerard B.; Chemburkar, Sanjay R.; Marsh, Kennan C.; Waring, Jeffrey F.; Hui, Julia Y.; Chen, Jinhua; Curzon, Peter; Grayson, George K.; Komater, Victoria A.; Ku, Yiyin; Lockwood, Mark; Miner, Holly M.; Nikkel, Arthur L.; Pan, Jia Bao; Pu, Yu-Ming; Wang, Lei; Bennani, Youssef; Jolly, Robert; Sullivan, James P.; Decker, Michael W. (Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL (US)); Bennani, Youssef (Vertex Pharmaceuticals, Cambridge, MA 01239 (US)); Jolly, Robert (Lilly Research Labs., Greenfield, IN 46104 (US)); Decker, Michael W. (Neuroscience Research, Department R4N5, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064-6125 (US)); Durmuller, Niklaus; Roux, Sylvain (Porsolt and Partners Pharmacology, Le Genest-Saint-Isle (FR))  
 EMAIL: michael.w.decker@abbott.com  
 Epilepsia (Sep 2005) Volume 46, Number 9, pp. 1349-1361, 33 refs.  
 CODEN: EPILAK ISSN: 0013-9580 E-ISSN: 1528-1167  
 DOI: 10.1111/j.1528-1167.2005.02905.x

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## COUNTRY OF PUBLICATION:

## DOCUMENT TYPE:

## LANGUAGE:

## SUMMARY LANGUAGE:

## ENTRY DATE:

United States of America

Journal; Article

English

English

Entered STN: 3 Feb 2009

Last updated on STN: 3 Feb 2009

Preclinical profiling and safety studies of **ABT-769**:

A compound with potential for broad-spectrum antiepileptic activity

## ST

**Absence seizures; ABT-769; Animal seizure models;** Anticonvulsant drugs; **Kindled amygdala seizures;** Maximal electroshock; Pentylentetrazol; Valproic acid

## AB

Purpose: The objective of this study was to characterize the antiseizure and safety profiles of **ABT-769** [(R)-N-(2-amino-2-oxoethyl)spiro[2,5]octane-1- carboxamide]. Methods: **ABT-769** was tested for protection against maximal electroshock and pentylentetrazol-induced **seizures** in the mouse and for suppression of electrically kindled amygdala **seizures** and spontaneous absence-like **seizures** in the rat. The central nervous system safety profile was evaluated by using tests of motor coordination and inhibitory avoidance. . . . was assessed in vitro by using a mitochondrial fatty acid  $\beta$ -oxidation assay. Teratogenic potential was assessed in the mouse. Results: **ABT-769** blocked maximal electroshock, subcutaneous pentylentetrazol and intravenous pentylentetrazol-induced **seizures** with median effective dose (ED 50 ) values of 0.25, 0.38, and 0.11 mmol/kg, p.o., respectively. No tolerance was evident in the intravenous pentylentetrazol test after twice-daily dosing of **ABT-769** (0.3 mmol/kg, p.o.) for 4 days. **ABT-769** blocked absence-like spike-wave discharge (ED 50 , 0.15 mmol/kg, p.o.) and shortened the cortical and amygdala afterdischarge duration of kindled **seizures** (1 and 3 mmol/kg, p.o.). The protective indices (ED 50 Rotorod impairment/ED 50 **seizure** protection) were 4.8, 3.2, and 10.9 in the maximal electroshock, subcutaneous pentylentetrazol and intravenous pentylentetrazol **seizure** tests, respectively. **ABT-769** did not affect inhibitory avoidance performance (0.1-1 mmol/kg, p.o.). **ABT-769** did not affect mitochondrial fatty acid  $\beta$ -oxidation or induce neural tube defects. Conclusions: **ABT-769** is an efficacious antiseizure agent in animal models of **convulsive**

and nonconvulsive **epilepsy** and has a favorable safety profile.  
**ABT-769** has a broad-spectrum profile like that of valproic acid. Its profile is clearly different from those of carbamazepine, phenytoin, lamotrigine, topiramate, vigabatrin, and tiagabine. .COPYRG.T. 2005 International League Against **Epilepsy**

L10 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2004:857165 CAPLUS

DOCUMENT NUMBER: 141:325759

TITLE: Spirocyclopropyl amides and acids and their therapeutic applications

INVENTOR(S): Bennani, Youseff L.; Bunnelle, William H.; Chang, Sou-Jen; Chemburkar, Sanjay R.; Chen, Jinhua; Dart, Michael J.; Fernando, Dilinip; Ku, Yi-Yin; Lockwood, Mark; Wang, Lei

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 27 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE       |
|------------------------|------|----------|-----------------|------------|
| US 20040204396         | A1   | 20041014 | US 2003-691095  | 20031022   |
| PRIORITY APPLN. INFO.: |      |          | US 2002-420286P | P 20021022 |

OTHER SOURCE(S): MARPAT 141:325759

AB . . . = H, alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycle, heterocyclealkyl; R3, R4 = H, alkenyl, alkyl, etc.) for the treatment of **epilepsy**, bipolar disorder, psychiatric disorders, migraine, pain, or movement disorders, and to provide neuroprotection. Representative compds. exhibited anticonvulsant ED50s in the . . .

ST . . . treatment spirocyclopropyl acid amide; psychiatric disorder treatment spirocyclopropyl amide acid; pain treatment spirocyclopropyl amide acid; migraine treatment spirocyclopropyl amide acid; **epilepsy** treatment spirocyclopropyl amide acid

IT Mental and behavioral disorders  
 (bipolar disorder, treatment of; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT Headache  
 (migraine, treatment of; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT Nerve, disease  
 (neuropathy, pain, treatment of; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT Cytoprotective agents  
 Nervous system agents  
 (neuroprotective agents; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT Inflammation  
 (pain, treatment of; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

IT Drug delivery systems

- (prodrugs; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
- IT Analgesics  
Anticonvulsants  
Antimigraine agents  
Mammalia  
(spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
- IT **Epilepsy**  
Mental and behavioral disorders  
Movement disorders  
Pain  
(treatment of; spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
- IT 17202-86-7P, Spiro[2.5]octane-1-carboxylic acid 17202-94-7P, Spiro[2.4]heptane-1-carboxylic acid 680618-92-2P, (1S)-N-((1S)-2-Amino-1-methyl-2-oxoethyl)spiro[2.5]octane-1-carboxamide 680618-93-3P, (1R)-N-((1S)-2-Amino-1-methyl-2-oxoethyl)spiro[2.5]octane-1-carboxamide 680618-94-4P 680618-96-6P 680618-99-9P 680619-02-7P, 2-Methylspiro[2.5]octane-1-carboxylic acid 680619-04-9P, 5,7-Dimethylspiro[2.5]octane-1-carboxylic acid 680619-06-1P, 6-tert-Butylspiro[2.5]octane-1-carboxylic acid 680619-08-3P, 2-Methylspiro[2.4]heptane-1-carboxylic acid 680619-11-8P, 3,3-Dimethylspiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxylic acid 680619-14-1P, 4-Methylspiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxylic acid 680619-21-0P, Spiro[2.6]nonane-1-carboxylic acid 680619-24-3P 680619-30-1P 680619-41-4P, 5,5,7,7-Tetramethylspiro[2.5]octane-1-carboxylic acid 680619-52-7P, Spiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxylic acid  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
- IT 680619-19-6, Spiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxamide 680619-22-1, Spiro[2.6]nonane-1-carboxamide  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
(spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
- IT 17202-88-9P, Spiro[2.5]octane-1-carboxamide 17202-96-9P, Spiro[2.4]heptane-1-carboxamide 680618-91-1P, N-(2-Amino-2-oxoethyl)spiro[2.5]octane-1-carboxamide 680618-95-5P, (1S)-N-(2-Amino-2-oxoethyl)spiro[2.5]octane-1-carboxamide 680618-98-8P, N-(2-Amino-2-oxoethyl)spiro[2.4]heptane-1-carboxamide 680619-00-5P 680619-01-6P 680619-03-8P, N-(2-Amino-2-oxoethyl)-2-methylspiro[2.5]octane-1-carboxamide 680619-05-0P, N-(2-Amino-2-oxoethyl)-5,7-dimethylspiro[2.5]octane-1-carboxamide 680619-07-2P, N-(2-Amino-2-oxoethyl)-6-tert-butylspiro[2.5]octane-1-carboxamide 680619-09-4P, 2-Methylspiro[2.4]heptane-1-carboxamide 680619-10-7P, N-(2-Amino-2-oxoethyl)-2-methylspiro[2.4]heptane-1-carboxamide 680619-13-0P, N-(2-Amino-2-oxoethyl)-3,3-dimethylspiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxamide 680619-16-3P, 4-Methylspiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxamide 680619-17-4P, N-(2-Amino-2-oxoethyl)-4-methylspiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxamide 680619-18-5P, Spiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxylic

- acid 680619-20-9P, N-(2-Amino-2-oxoethyl)spiro(bicyclo[2.2.1]heptane-2,1'-cyclopropane)-2'-carboxamide 680619-23-2P, N-(2-Amino-2-oxoethyl)spiro[2.6]nonane-1-carboxamide 680619-26-5P 680619-28-7P 680619-33-4P 680619-35-6P 680619-37-8P, N-(3-Amino-3-oxopropyl)spiro[2.5]octane-1-carboxamide 680619-43-6P, 5,5,7,7-Tetramethylspiro[2.5]octane-1-carboxamide 680619-45-8P, N-(2-Amino-2-oxoethyl)-5,5,7,7-tetramethylspiro[2.5]octane-1-carboxamide 680619-47-0P, [(Spiro[2.5]oct-1-ylcarbonyl)amino]acetic acid 680619-53-8P, N-(2-Amino-2-oxoethyl)spiro(bicyclo[3.2.0]heptane-6,1'-cyclopropane)-2'-carboxamide 680619-54-9P, (1R)-N-((2R)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide 680619-55-0P, (1S)-N-((2R)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide 680619-56-1P, (1R)-N-((2S)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide 680619-57-2P, (1S)-N-((2S)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
- IT 680618-97-7, (1R)-N-(2-Amino-2-oxoethyl)spiro[2.5]octane-1-carboxamide 680619-12-9, 3,3-Dimethylspiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxamide 680619-39-0, Spiro[2.7]decane-1-carboxylic acid 680619-58-3 680619-59-4 680619-60-7, 2-Methylspiro[2.5]octane-1-carboxamide 680619-61-8, 5,7-Dimethylspiro[2.5]octane-1-carboxamide 680619-62-9, 6-tert-Butylspiro[2.5]octane-1-carboxamide 680619-63-0, Spiro[2.7]decane-1-carboxamide 680619-64-1, N-(2-Amino-2-oxoethyl)spiro[2.7]decane-1-carboxamide 680619-65-2, Spiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxamide RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
- IT 623-73-4, Ethyl diazoacetate 1192-37-6, Methylenecyclohexane 1336-21-6, Ammonium hydroxide 1668-10-6, 2-Aminoacetamide hydrochloride 2799-16-8, (R)-1-Amino-2-propanol 2799-17-9, (S)-1-Amino-2-propanol 4726-85-6, 3-Aminopropanamide 4832-17-1, 2-Decalone 5680-79-5, Glycine methyl ester hydrochloride 33208-99-0, (2S)-2-Aminopropanamide hydrochloride 33883-43-1 110253-44-6 646990-40-1 770728-66-0 770728-67-1 770728-68-2 770728-69-3 770728-70-6 770728-71-7 770728-72-8 770728-74-0 770728-75-1 RL: RCT (Reactant); RACT (Reactant or reagent) (spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)
- IT 17202-87-8P 58396-40-0P, 2-Methylenedecahydronaphthalene 770728-73-9P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (spirocyclopropyl amides and acids for neuroprotection and treatment of **epilepsy**, bipolar disorders, migraine,)

L10 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2004:331780 CAPLUS

DOCUMENT NUMBER: 140:338974

TITLE: Preparation of spirocyclopropyl amides and acids as anticonvulsants

INVENTOR(S): Bennani, Youssef L.; Bunnelle, William H.; Chang, Sou-Jen; Chemburkar, Sanjay R.; Chen, Jinhua; Dart, Michael J.; Fernando, Dillinie P.; Ku, Yi-Yin; Lockwood, Mark; Wang, Lei

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 27 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| US 20040077616  | A1   | 20040422 | US 2002-277266  | 20021022 |
| CA 2502906  | A1   | 20040506 | CA 2003-2502906 | 20031022 |
| WO 2004037240   | A1   | 20040506 | WO 2003-US33688 | 20031022 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, NI, TD, TG<br>AU 2003283011 A1 20040513 AU 2003-283011 20031022<br>EP 1558230 A1 20050803 EP 2003-774943 20031022<br>EP 1558230 B1 20081231<br>R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK<br>JP 2006513156 T 20060420 JP 2004-547101 20031022<br>AT 418973 T 20090115 AT 2003-774943 20031022<br>MX 2005004267 A 20050726 MX 2005-4267 20050421<br>PRIORITY APPLN. INFO.: US 2002-277266 A 20021022<br>WO 2003-US33688 W 20031022 |      |          |                 |          |

OTHER SOURCE(S): MARPAT 140:338974

AB . . . saponified to give II. Representative examples of I exhibit ED50 = 0.84 - 0.35 mmol/kg in the s.c. pentylenetetrazole (PTZ) seizure model. I are useful in the treatment of epilepsy, bipolar disorder, psychiatric disorders, migraine, pain, or movement disorders, and to provide neuroprotection.

IT Analgesics

Anti-inflammatory agents

Anticonvulsants

Antimigraine agents

Epilepsy

Human

Pain

(preparation of spirocyclopropyl amides and acids as anticonvulsants)

IT 17202-88-9P, Spiro[2.5]octane-1-carboxamide 17202-96-9P, Spiro[2.4]heptane-1-carboxamide 680618-95-5P, (1S)-N-(2-Amino-2-oxoethyl)spiro[2.5]octane-1-carboxamide **680618-97-7P**, (1R)-N-(2-Amino-2-oxoethyl)spiro[2.5]octane-1-carboxamide 680618-98-8P, N-(2-Amino-2-oxoethyl)spiro[2.4]heptane-1-carboxamide 680619-00-5P 680619-01-6P 680619-03-8P, N-(2-Amino-2-oxoethyl)-2-methylspiro[2.5]octane-1-carboxamide 680619-05-0P, N-(2-Amino-2-oxoethyl)-5,7-dimethylspiro[2.5]octane-1-carboxamide 680619-07-2P, N-(2-Amino-2-oxoethyl)-6-tert-butylspiro[2.5]octane-1-carboxamide 680619-09-4P, 2-Methylspiro[2.4]heptane-1-carboxamide 680619-10-7P, N-(2-Amino-2-oxoethyl)-2-methylspiro[2.4]heptane-1-carboxamide 680619-12-9P, 3,3-Dimethylspiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxamide 680619-13-0P, N-(2-Amino-2-oxoethyl)-3,3-

dimethylspiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxamide  
 680619-16-3P, 4-Methylspiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-  
 carboxamide 680619-17-4P, N-(2-Amino-2-oxoethyl)-4-  
 methylspiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxamide  
 680619-19-6P, Spiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-  
 carboxamide 680619-20-9P, N-(2-Amino-2-  
 oxoethyl)spiro[bicyclo[2.2.1]heptane-2,1'-cyclopropane]-2'-carboxamide  
 680619-22-1P, Spiro[2.6]nonane-1-carboxamide 680619-23-2P,  
 N-(2-Amino-2-oxoethyl)spiro[2.6]nonane-1-carboxamide 680619-26-5P  
 680619-28-7P 680619-33-4P 680619-35-6P 680619-37-8P,  
 N-(3-Amino-3-oxopropyl)spiro[2.5]octane-1-carboxamide 680619-43-6P,  
 5,5,7,7-Tetramethylspiro[2.5]octane-1-carboxamide 680619-45-8P,  
 N-(2-Amino-2-oxoethyl)-5,5,7,7-tetramethylspiro[2.5]octane-1-carboxamide  
 680619-47-0P, [(Spiro[2.5]oct-1-ylcarbonyl)amino]acetic acid  
 680619-49-2P, (S)-[[Spiro[2.5]oct-1-ylcarbonyl]amino]acetic acid  
 680619-51-6P, (R)-[[Spiro[2.5]oct-1-ylcarbonyl]amino]acetic acid  
 680619-53-8P, N-(2-Amino-2-oxoethyl)spiro[bicyclo[3.2.0]heptane-6,1'-  
 cyclopropane]-2'-carboxamide 680619-54-9P,  
 (1R)-N-((2R)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide  
 680619-55-0P, (1S)-N-((2R)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide  
 680619-56-1P, (1R)-N-((2S)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide  
 680619-57-2P, (1S)-N-((2S)-2-Hydroxypropyl)spiro[2.5]octane-1-carboxamide  
 680619-58-3P, (S)-Spiro[2.5]octane-1-carboxamide 680619-59-4P,  
 (R)-Spiro[2.5]octane-1-carboxamide 680619-60-7P,  
 2-Methylspiro[2.5]octane-1-carboxamide 680619-61-8P,  
 5,7-Dimethylspiro[2.5]octane-1-carboxamide 680619-62-9P,  
 6-tert-Butylspiro[2.5]octane-1-carboxamide 680619-63-0P,  
 Spiro[2.7]decane-1-carboxamide 680619-64-1P,  
 N-(2-Amino-2-oxoethyl)spiro[2.7]decane-1-carboxamide 680619-65-2P,  
 Spiro[bicyclo[3.2.0]heptane-6,1'-cyclopropane]-2'-carboxamide  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (preparation of spirocyclopropyl amides and acids as anticonvulsants)

L10 ANSWER 5 OF 5 ADISINSIGHT COPYRIGHT (C) 2009 Adis Data Information BV on  
 STN

CN Research programme: antiepileptic therapies - Abbott Laboratories

CN **ABT 769; ABT-769**

CN (R)-N-(2-Amino-2-oxoethyl)spiro(2,5)octane-1-carboxamide

CC EPHMRA ATC CODE: **N3A Anti-Epileptics**

CC WHO ATC CODE: N03A-G Fatty acid derivatives

DSTA Preclinical, United States, **Epilepsy**

. . . antiepileptic therapies which have a better safety and tolerability  
 profile than the current generation of drugs, the lead compound is  
**ABT 769** a valproic acid analogue with possible broad  
 spectrum applications. The glycineamide moiety of **ABT 769**  
 , in analogy with the nonteratogenic valproic acid derivative TV-1901 was  
 incorporated into **ABT 769** to increase antiseizure  
 efficacy and reduce the likelihood for induction of neural tube  
 defects/1/.

TX Adverse Events:

Animal studies: in a preclinical study using mice and rats **ABT**

**769** showed a favourable safety profile. **ABT 769**

did not affect mitochondrial fatty acid -oxidation or induce neural tube  
 defects. Dosages of 4 and 8 mmol/kg od were. . .

TX PHARMACOLOGY:

Pharmacodynamics (**Epilepsy** and **Seizure** Disorders):



Animal studies: **ABT 769** was an efficacious antiseizure agent in animal models of convulsive and nonconvulsive epilepsy. **ABT 769** was tested for protection against maximal electroshock and pentylenetetrazol-induced seizures in the mouse, as well as suppression of electrically kindled amygdala seizures and spontaneous absense-like seizures in rats. **ABT 769** blocked maximal electroshock, subcutaneous pentylenetetrazol and IV pentylenetetrazol-induced seizures with ED sub(50) values of 0.25, 0.38 and 0.11 mmol/kg PO respectively. No tolerance was evident in the IV pentylenetetrazol test after bid dosing of **ABT 769** at 0.3 mmol/kg PO for four-days. **ABT 769** blocked absense like spike-wave discharge at an ED sub(50) value of 0.15 mmol/kg, and shortened the cortical and amygdala after-discharge duration of kindled seizures at ED sub(50) values of 1 and 3 mmol/ kg PO, respectively). **ABT 769** did not affect inhibitory avoidance performance at 0.1-1 mmol/kg PO/1/.

=> d his

(FILE 'HOME' ENTERED AT 14:34:42 ON 09 JUN 2009)

FILE 'REGISTRY' ENTERED AT 14:34:56 ON 09 JUN 2009

L1 1 S ABT 769/CN

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CAPLUS, DDFB, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIODASE, IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, KOSMET, LIFESCI, MEDLINE, NAPRALERT, NLDB, NUTRACEUT, PASCAL, PCTGEN, PHARMAML, ...' ENTERED AT 14:35:15 ON 09 JUN 2009

L2 20 S L1 OR ABT 769

L3 772019 S EPILEP?

L4 228807 S CONVULS?

L5 581577 S SEIZURE

L6 1189744 S L3 OR L4 OR L5

L7 18 S L6 AND L2

L8 2 S L2 NOT L7

L9 2 DUP REM L8 (0 DUPLICATES REMOVED)

L10 5 DUP REM L7 (13 DUPLICATES REMOVED)